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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053,929	01/22/2002	Julie Straub	ACU 109 CIP	7093

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Pabst Patent Group LLP
1545 PEACHTREE STREET NE
SUITE 320
ATLANTA, GA 30309

EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1613	

MAIL DATE	DELIVERY MODE
08/20/2010	PAPER

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The time period for reply, if any, is set in the attached communication.

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JULIE STRAUB, DAVID ALTREUTER, HOWARD BERNSTEIN, DONALD E. CHICKERING III, SARWAT KHATTAK, and GREG RANDALL,
Appellants[1]

Appeal 2009-013564
Application 10/053,929
Technology Center 1600

Before CAROL A. SPIEGEL, LORA M. GREEN, and MELANIE L. McCOLLUM, *Administrative Patent Judges.*

SPIEGEL, *Administrative Patent Judge.*

DECISION ON APPEAL[2]

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[1] The real parties in interest are ACUSPHERE, INC. and CEPHALON, INC. (Appeal Brief filed 9 December 2008 ("App. Br.") at 2). This decision also cites to the Examiner's Answer mailed 17 March 2009 ("Ans."), and the Reply Brief to the Examiner's Answer filed 18 May 2009 ("Reply Br.").

[2] The two month period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

Appellants appeal under 35 U.S.C. § 134(a) from the Examiner's final rejection of all pending claims, claims 16-21 and 34, as obvious under 35 U.S.C. § 103(a) over Unger[3] (App. Br. 2; Ans. 3-4). We have jurisdiction under 35 U.S.C § 134. We REVERSE.

I. Statement of the Case

The subject matter on appeal is directed to a method of making a pharmaceutical composition having a porous matrix formed of at least one hydrophilic or hydrophobic excipient and microparticles of a drug, wherein the matrix and the microparticles have specifically defined physical properties. The microparticles have a mean diameter of between about 0.1 and 5 μm and total surface area greater than about 0.5 m^2/mL, while the matrix is in a dry powder form and has a transaxial pressure ("TAP") density less than or equal to 1.0 g/mL and a surface area greater than or equal to 0.2 m^2/g. Claims 16, 18, 21, and 22 are illustrative and read (App. Br. 21-22):

> 16. A method for making a pharmaceutical composition comprising a porous matrix formed of at least one hydrophilic or hydrophobic excipient and microparticles of a drug, wherein the microparticles have a mean diameter between about 0.1 and 5 μm and a total surface area greater than about 0.5 m^2/mL, and wherein the dry porous matrix is in a dry powder form having a TAP density less than or equal to 1.0 g/mL and having a total surface area of greater than or equal to 0.2 m^2/g, comprising
>
> (a) dissolving a drug in a volatile solvent to form a drug solution,

[3] US Patent Application Publication 2001/0018072 A1, *Solid Matrix Therapeutic Compositions,* Evan C. Unger, published 30 August 2001 ("Unger").

(b) combining at least one volatile solid pore forming agent with the drug solution to form an emulsion, suspension, or second solution,

(c) incorporating at least one excipient into the emulsion, suspension, or second solution, wherein the emulsion is selected from the group consisting of hydrophobic and hydrophilic excipients which enhance dissolution rate, which stabilize drug in amorphous form by preventing crystallization, and which stabilize drug in crystalline form by inhibiting crystal growth, and

(d) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug and excipient.

18. The method of claim 16 wherein the excipients are selected from the group consisting of polymers, amino acids, wetting agents, sugars, preservatives, pegylated excipients, tonicity agents, and combinations thereof.

20. The method of claim 16 wherein the pore forming agent is a volatile salt.

21. The method of claim 20 wherein the volatile salt is selected from the group consisting of ammonium bicarbonate, ammonium acetate, ammonium chloride, ammonium benzoate, and mixtures, thereof.

Essentially, the Examiner's position is that Unger discloses mixing the same reagents, i.e., drug (bioactive material), ammonium carbonate (a volatile pore forming agent), surfactant (excipient), and solvent (volatile solvent to dissolve the drug), and then removing the solvent by lyophilizing or spray drying to form a porous matrix and, therefore, the claimed method

is obvious (Ans. 3-4).[4] The Examiner acknowledges that Unger does not teach performing the method steps in the claimed order, but states that "selection of any order performing process steps or mixing ingredients is prima facie obvious in the absence of new and unexpected results" (*id.* at 4).

Appellants argue that Unger not only fails to teach or suggest the method of claim 16, but also that Unger fails to teach or suggest forming a porous matrix having the specifically defined physical properties recited in claim 16 (App. Br. 9, 13-16, 19; Reply Br. 1-4). Appellants further argue that Unger does not disclose the claimed method steps. For example, Unger uses a solvent to form an emulsion containing a drug, not a drug-containing solution as recited in claim 16, step (a) (App. Br. 9-10; Reply Br. 6). Appellants also argue that Unger uses a liquid blowing agent, not a volatile salt, to form pores as recited in claims 16, step (b), 19 and 20 (App. Br. 11-12, 16-17; Reply Br. 6-7). In addition, Appellants argue the Unger fails to teach or suggest the excipients required by claim 18 (App. Br. 16).

At issue is whether or not Unger teaches or suggests the specific method steps and in the order set forth in the claims to produce a porous matrix having generally the same the composition and physical properties as the porous matrix recited in the claims.

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[4] According to the Examiner, "the specific method steps are known in the art for the production of powder formulation (for example, column 2, lines 49-51; column 3, line 30 and column 9, line 41, of US 5,976,574 issued to Gordon …)" (Ans. 4). Gordon is not included in any of the statements of rejection or identified as evidence relied upon by the Examiner ("Gordon is not used to reject the claims" (*id.* at 6). Thus, Gordon is not properly before us and arguments based on Gordon have not been considered in reaching our decision. *In re Hoch*, 428 F.2d 1341, 1342 n.3 (CCPA 1970).

II. Findings of Fact

The following findings of fact ("FF") are supported by a preponderance of the evidence of record.

A. Unger

[1] Unger discloses

> [a] solid porous matrix comprising a solvent, a surfactant and a therapeutic … processed by controlled drying, or controlled agitation and controlled drying by a number of methods known in the art. The methods of drying include … spray drying, lyophilization, and vacuum drying. Agitation methods include … shaking, vortexing, and ball milling.
>
> Most preferably a solid porous matrix comprising a surfactant and a therapeutic is prepared such that a solvent, a surfactant, and a therapeutic are combined *to form an emulsion in the form of a random aggregate*. In the case of spray drying, the emulsion or colloidal suspension, is placed into association with a blowing agent such as methylene chloride … the solvent, surfactant, and therapeutic, may be combined and the blowing agent subsequently added thereto. Alternatively, the ingredients may be separated and combined in a stream of air together with the blowing agent. The blowing agent is stabilized by the surfactant …. Additionally, some nonpolar drugs [sic] emulsions may contain an oil to effect solubilization. As the suspension or emulsion is then spray dried, the drug dries and *the blowing agent and solvent are removed tending to form microcavities* within the drug crystals. The surfactants typically tend to adsorb to the surface of the porous drug crystal lattice. The resulting powdered crystalline drug material may be stored under a head space of the desired gas. Preferably

> an insoluble gas … such a perfluorobutane. This results in crystalline drug matrices imbibing insoluble gas. When the drug matrices are resuspended, the result is crystalline matrices of drug surrounded by a film of gas/gaseous precursor material and surfactant. [Unger ¶¶ 183-184, emphasis added.]

[2] According to Unger, the solvent is a "suspending medium" for associating the surfactant with the drug and the drug is "typically only marginally soluble in the solvent" (*id.* at ¶ 75).

[3] Further according to Unger, a gas or gaseous precursor is an optional component of the matrix composition (*id.* at ¶ 13) and the gaseous precursor may be selected to form the gas *in situ* in a targeted tissue or fluid, *in vivo* upon entering the patient or animal, prior to use, or during storage or manufacture (*id.* at ¶ 214).

[4] According to Unger, "[t]he gas provides the solid porous matrix will [sic, with] enhanced reflectivity, particularly in connection with a porous matrix in which the gas is entrapped within the solid porous solid matrix …[which] may increase their effectiveness as contrast agents or delivery vehicles" (*id.* at ¶ 160).

[5] Exemplary gaseous precursors include ammonium (bi)carbonates and perfluorocarbons (*id.* at ¶¶ 167-168).

B. The '929 Specification ("Spec.")

[6] According to the '929 Specification, when a solid pore forming agent is combined with a solution containing a drug,

> it is dissolved either directly in the drug solution to form a solution of drug/pore forming agent, or it is first dissolved in a second solvent which is immiscible with the drug solvent to form a

> solution which subsequently is emulsified with the drug solution to form droplets of the pore forming agent solution dispersed throughout the drug solution. A solid pore forming agent alternatively can be added directly to the drug solution as solid particulates, preferably between about 100 nm and 10 µm in size, to form a suspension of pore forming agent in the drug solution. [Spec. 21:23-31.]

III. Discussion

A. Legal principles

"The test of obviousness *vel non* is statutory. It requires that one compare the claim's 'subject matter as a whole' with the prior art 'to which said subject matter pertains.' 35 U.S.C. § 103. The inquiry is thus highly fact-specific by design. This is so 'whether the invention be a process for making or a process of using, or some other process.'" *In re Brouwer*, 77 F.3d 422, 425 (Fed. Cir. 1996). In *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 418 (2007) (citing *In re Kahn*, 441 F.3d 997, 988 (Fed. Cir. 2006)), the Supreme Court noted that "[t]o facilitate review, this [obviousness] analysis should be made explicit."

Furthermore, obviousness requires a suggestion of all limitations in a claim. *In re Royka*, 490 F.2d 981, 985 (CCPA 1974). Generally, a preamble is not accorded any patentable weight when it merely recites the purpose of a process and where the body of a claim does not depend on the preamble for completeness. *In re Hirao*, 535 F.2d 67, 70 (CCPA 1976). However, where the claim preamble is "necessary to give life, meaning, and vitality" to the claim, it is accorded patentable weight. *Kropa v. Robie*, 187 F.2d 150, 152 (CCPA 1951).

Finally, "[t]he materials used in a claimed process as well as the result obtained therefrom, must be considered along with the specific nature of the process, and the fact that new or old, obvious or nonobvious, materials are used or result from the process are only factors to be considered, rather than conclusive indicators of the obviousness or nonobviousness of a claimed process." *In re Dillon*, 919 F.2d 688, 695 (Fed. Cir. 1990).

B. Analysis

Here, the preamble of claim 16 is "necessary to give life, meaning, and vitality" to the claimed process because it defines the porous matrix recited in step (d), i.e., claim 16 depends upon its preamble for completeness. According to the Examiner, "the goal of the [claimed] process is the formation of a porous matrix and the end result of Unger's process is that a porous matrix is prepared" (Ans. 5). However, the goal of the process of claim 16 is more specific, i.e., it is to form a porous matrix comprising microparticles of a drug wherein both the matrix and the microparticles have specifically defined physical properties. The Examiner has failed to provide either a reasoned analysis or a factual basis for concluding that the method of Unger would have reasonably been expected to produce a porous matrix with the physical properties recited in claim 16. In other words, the Examiner has failed to address every limitation in the claimed method.

In addition, both the materials used in a process as well as the results obtained therefrom must be considered in determining the obviousness or nonobviousness of a claimed process. Here, for example, the claimed method recites "dissolving a drug in a volatile solvent to form a drug solution." While Unger teaches use of a volatile solvent, the result obtained

therefrom is different. Instead of forming a drug solution, Unger forms "an emulsion in the form of a random aggregate" (FF 1). According to Unger, the drug is "typically only marginally soluble in the solvent" (FF 2). As pointed out by Appellants (Reply Br. 3), this is a difference in kind, not in order, of a method step. To wit, the Examiner has not explained why one of ordinary skill in the art would have used a solvent in which a drug dissolved, i.e., was soluble, in place of a solvent in which the drug was marginally soluble as taught by Unger. We are not persuaded by the Examiner's statement that the "organic solvent in claim 16 is generic encompassing any and all organic solvent" (Ans. 5) because the statement ignores the relationship between the solvent and the drug taught by Unger.

Similarly, while Unger uses ammonium (bi)carbonate as a gaseous precursor (FF 5), Unger also teaches that the gaseous precursor is optional and may be selected to form the gas *in situ* in a targeted tissue or fluid, *in vivo* upon entering the patient or animal, prior to use, or during storage or manufacture (FF 3). The Examiner has not explained why one of ordinary skill in the art would have chosen an optional component, which may or may not be reactive during storage or manufacture, to form pores in the resulting matrix, particularly in view of Unger's express teaching that pores are formed from the drug suspension or emulsion during drying when blowing agent and solvent are removed (FF 1).

Therefore, for at least these reasons, we reverse the rejection of claims 16-21 and 34 under § 103(a) over Unger. Based upon the evidence of record, Unger fails to teach or suggest the specific method steps and in the order set forth in the claims to produce a porous matrix having generally the

same the composition and physical properties as the porous matrix recited in the claims.

IV. Order

Upon consideration of the record, and for the reasons given, it is

ORDERED that the decision of the Examiner to reject claims 16-21 and 34 as unpatentable under 35 U.S.C. § 103(a) over Unger is REVERSED.

REVERSED

cdc

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